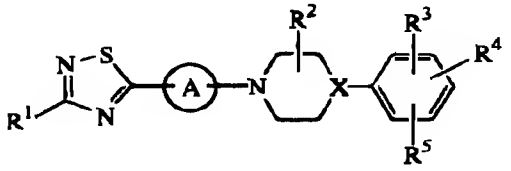
*Note: Applicant uses:*

- ~~***Bold cross-out text***~~ *to indicate deletions;*
- ***Bold underline text*** *to indicate additions.*

**Amendments to the Claims:**

1. (Previously Amended) A compound of formula (I),



(I),

the *N*-oxide forms, the pharmaceutically acceptable acid addition salts and stereochemically isomeric forms thereof, wherein

X is N;

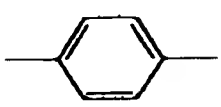
$R^1$ is hydrogen, $C_{1-6}$alkyl, $C_{1-6}$alkyloxy, $C_{1-6}$alkylthio, amino, mono- or di($C_{1-6}$alkyl)amino, $Ar^1$, $Ar^1NH$-, $C_{3-6}$cycloalkyl, hydroxymethyl or benzyloxymethyl;

$R^2$ is hydrogen, $C_{1-6}$alkyl, amino, aminocarbonyl, mono- or di($C_{1-6}$alkyl)amino, $C_{1-6}$alkyloxycarbonyl, $C_{1-6}$alkylcarbonylamino, hydroxy or $C_{1-6}$alkyloxy;

$R^3$, $R^4$ and $R^5$ are each independently selected from hydrogen, halo, $C_{1-6}$alkyl, $C_{1-6}$alkyloxy, trifluoromethyl, nitro, amino, cyano, azido, $C_{1-6}$alkyloxy$C_{1-6}$alkyl, $C_{1-6}$alkylthio, $C_{1-6}$alkyloxycarbonyl or $Het^1$;

 is $Ar^2$ or $Het^2$;

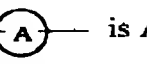
$Ar^1$ is phenyl; phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, $C_{1-6}$alkyl, $C_{1-6}$alkyloxy, trihalomethyl, amino or nitro;

$Ar^2$ is  ;  substituted with 1, 2 or 3 substituents each independently selected from halo, $C_{1-6}$alkyl, $C_{1-6}$alkyloxy, trihalomethyl, amino or nitro;

$Het^1$ is a monocyclic heterocycle selected from oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, thiadiazolyl or oxazolinyl; and each monocyclic heterocycle may optionally be substituted on a carbon atom with $C_{1-4}$alkyl; and

$Het^2$ is a monocyclic heterocycle selected from thiadiazolyl, pyridinyl, pyrimidinyl or pyrazinyl; and each monocyclic heterocycle may optionally be substituted on a carbon atom with 1 or 2 substituents each independently selected from halo, $C_{1-4}$alkyl, $C_{1-4}$alkyloxy, nitro or trifluoromethyl.

2. (Previously Amended) A compound according to claim 1 wherein $R^1$ is hydrogen, $C_{1-6}$alkyl, amino or di($C_{1-6}$alkyl)amino; $R^2$ is hydrogen; $R^3$, $R^4$ and $R^5$ are each independently selected from hydrogen, halo, $C_{1-6}$alkyl, $C_{1-6}$alkyloxy, trifluoromethyl, nitro or $C_{1-6}$alkyloxycarbonyl.

3. (Previously Amended) A compound according to claim 1 wherein $R^1$ is hydrogen, $C_{1-4}$alkyl or di($C_{1-4}$alkyl)amino; $R^2$ is hydrogen; $R^3$, $R^4$ and $R^5$ are each independently selected from hydrogen, halo, $C_{1-4}$alkyl, $C_{1-4}$alkyloxy or trifluoromethyl; and the bivalent radical  is $Ar^2$ or $Het^2$ wherein $Ar^2$ is phenyl and $Het^2$ is thiadiazolyl, pyridinyl, pyrimidinyl or pyrazinyl.

4. (Previously Amended) A compound according to claim 1 wherein $R^1$ is methyl, $R^2$ is hydrogen, $R^3$ and $R^4$ are hydrogen and $R^5$ is trifluoromethyl.

5. (Previously Amended) A compound according to claim 1 wherein the compound is

1-[4-(3-methyl-1,2,4-thiadiazol-5-yl)phenyl]-4-[3-(trifluoromethyl)phenyl]-piperazine; or
1-[5-(3-methyl-1,2,4-thiadiazol-5-yl)-2-pyridinyl]-4-[3-(trifluoromethyl)phenyl]-piperazine; a stereoisomeric form, a pharmaceutically acceptable acid addition salt, or an N-oxide thereof.

6. (Previously Amended) A composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as claimed in claim 1.

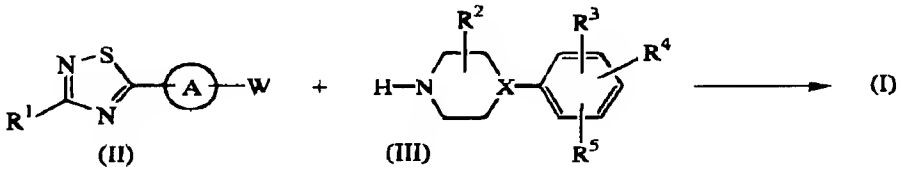
7. (Previously Cancelled).

8. (Previously Cancelled).

9. (Previously Cancelled).

10. **(Currently Amended)** A process of preparing a compound as claimed in claim 1, wherein

a) an intermediate of formula (II) is reacted with an intermediate of formula (III) in a reaction-inert solvent and, optionally in the presence of a suitable base;



(II) (III) (I)

b) an intermediate of formula (IV) is treated with hydroxylamino-O-sulfonic acid in a reaction-inert solvent, in the presence of a suitable base, thereby yielding compounds of formula (I-a), defined as compounds of formula (I) wherein $R^1$ is methyl;

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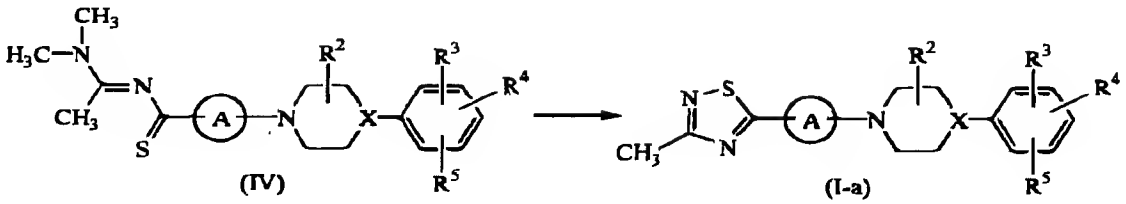
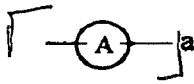


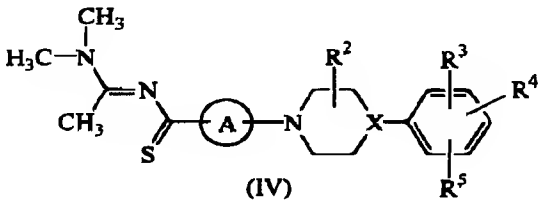
(IV) (I-a)

wherein in the above reaction schemes the radicals X, $R^1$, $R^2$, $R^3$, $R^4$, $R^5$ and

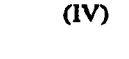
T,0203  are as defined in claim 1, and W is an appropriate leaving group;

c) ~~or, a compound of formula (I) is converted into another compound of formula (I) by art-known group transformation reactions;~~ or if desired, a compound of formula (I) is converted into a pharmaceutically acceptable acid addition salt **thereof**, or conversely, an acid addition salt of a compound of formula (I) is converted into a free base form **thereof** with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

11. A compound of formula (IV),



(IV)

an acid addition salt, a *N*-oxide form or a stereochemically isomeric form thereof, wherein X, $R^2$, $R^3$, $R^4$, $R^5$ and the bivalent radical  are as defined in claim 1.

D29 12. **(Currently Amended)** A process of preparing a compound of formula (IV) as claimed in claim 11, wherein

a) an intermediate of formula (IX) is treated with *N,N*-dimethylacetamide dimethyl acetal in a reaction-inert solvent, thereby yielding a compound of formula (IV);

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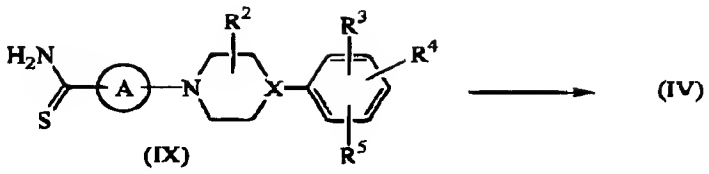


b) ~~or, a compound of formula (IV) is converted into another compound of formula (IV) by art known group transformation reactions;~~ or if desired~~,~~ a compound of formula (IV) is converted into an acid addition salt **thereof**, or conversely, an acid addition salt of a compound of formula (IV) is converted into a free base form **thereof** with alkali; and, if desired, preparing stereochemically isomeric forms thereof.

13. A method of treating angiogenesis dependent disorders comprising administering to a host in need thereof an effective amount of a compound of claim 1.

14. A method of treating angiogenesis dependent disorders comprising administering to a host in need thereof an effective amount of a compound of claim 2.

15. A method of treating angiogenesis dependent disorders comprising administering to a host in need thereof an effective amount of a compound of claim 3.

16. A method of treating angiogenesis dependent disorders comprising administering to a host in need thereof an effective amount of a compound of claim 4.

17. A method of treating angiogenesis dependent disorders comprising administering to a host in need thereof an effective amount of a compound of claim 5.

18. (Previously Amended) A compound according to claim 2 wherein $R^1$ is hydrogen, $C_{1-4}$alkyl or di($C_{1-4}$alkyl)amino; $R^2$ is hydrogen; $R^3$, $R^4$ and $R^5$ are each independently selected from hydrogen, halo, $C_{1-4}$alkyl, $C_{1-4}$alkyloxy or trifluoromethyl; and the bivalent

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radical  is $Ar^2$ or $Het^2$ wherein $Ar^2$ is phenyl and $Het^2$ is thiadiazolyl, pyridinyl, pyrimidinyl or pyrazinyl.

19. (Previously Amended) A compound according to claim 2 wherein $R^1$ is methyl, $R^2$ is hydrogen, $R^3$ and $R^4$ are hydrogen and $R^5$ is trifluoromethyl.

20. (Previously Amended) A compound according to claim 3 wherein $R^1$ is methyl, $R^2$ is hydrogen, $R^3$ and $R^4$ are hydrogen and $R^5$ is trifluoromethyl.

21-37. (Previously Cancelled).

38. (Previously Amended) A method of treating angiogenesis dependent disorders comprising administering to a host in need thereof an effective amount of

1-[4-(3-methyl-1,2,4-thiadiazol-5-yl)phenyl]-4-[3-(trifluoromethyl)phenyl]-piperazine;

or

1-[5-(3-methyl-1,2,4-thiadiazol-5-yl)-2-pyridinyl]-4-[3-(trifluoromethyl)phenyl]-piperazine; a stereoisomeric form, a pharmaceutically acceptable acid addition salt, or an N-oxide thereof.

## REMARKS

Claims 1-6,10-20 and 38 are pending in this application. The Examiner has allowed claims 1-6, 11, 13-20 and 38. Claims 10 and 12 are amended.

Support for the amendment to claims 10 and 12 is found in the Specification at pages 5-6.

### Rejection Under 35 U.S.C. §112, second paragraph

Claims 10 and 12 are rejected under 35 U.S.C. §112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention" (Office Action at page 2). Specifically, the Examiner asserts that it remains "unclear as to which ocmpound gets converted into which" in step (c) (Office Acton at 2).

Applicants have amended claims 10 and 12, without disclaimer or prejudice. Applicants respectfully submit that as amended claims 10 and 12 comport fully with the requirements of 35 U.S.C. §112, second paragraph, and accordingly, the rejection is rendered moot. Withdrawal of the rejection, and passage of the claims to allowance, is respectfully requested.

### Conclusion

Applicants respectfully request that a timely Notice of Allowance of claims 1-6,10-20 and 38 be issued in this case. The Examiner is cordially invited to contact the undersigned with any questions regarding this application.

Respectfully submitted,

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